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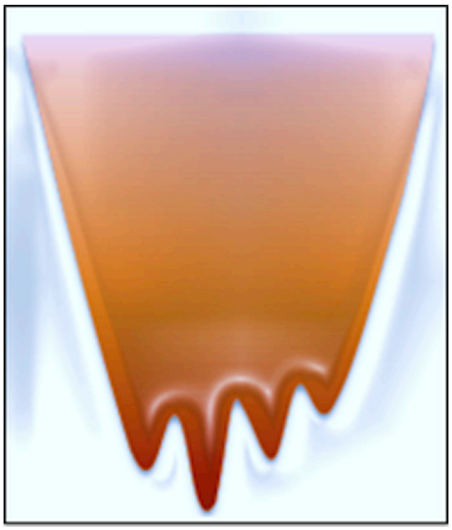
Chemistry & Biology

In This Issue

Perspective: Funneling the Function

PAGE 311

Simplified representations can be powerful. Capturing function is challenging because activation involves triggered dynamic shifts between states. Nussinov and Tsai show that simple funnel drawings capture and portray proteins by their cellular triggering mechanism, and create templates for function classification.



In Review: Vitamin D

PAGE 319

Vitamin D is essential for regulating numerous biologic processes through the widespread distribution of its receptor and activating enzymes. The review by Bikle examines vitamin D production and metabolism, its mechanisms of actions, and the clinical utility of its metabolites and analogs.

In Brief: Midchain Protein Arginylation

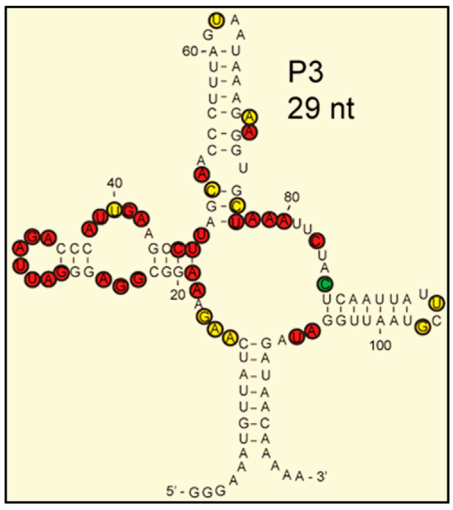
PAGE 331

Arginylation plays an important role in normal physiology; however, its action is poorly understood. Wang et al. find that arginyltransferase ATE1 can modify intact proteins on the side chains of Asp and Glu by chemistry that targets their carboxyl groups, thus clarifying the mechanism of arginylation in vivo.

In Brief: Target-Selective Phototherapy

PAGE 338

Type 2 cannabinoid receptor (CB_2R) is overexpressed in various types of cancers and emerging as an attractive target for cancer therapy. Zhang et al. report the first cancer phototherapy that uses a CB_2R–targeted photosensitizer which shows therapeutic effects only when bound to the target receptor.



Fluorescent SAM Analogs for HTS

PAGE 345

Many RNAs and proteins that bind S-adenosylmethionine (SAM) are of interest as drug targets. Hickey and Hammond describe the synthesis of fluorescent SAM analogs and validate that one of the analogs is useful in developing a high-throughput screen for competitive binders to SAM-I riboswitches.

"Dual Binder" Technology

PAGE 357

Protein-protein interactions and protein phosphorylation are crucial events in cell activation. In the "dual binder" technology developed by van Dieck et al., bispecific reagents are used to detect such events with high specificity. Dual binders achieve specificity through a cooperative binding effect.

Visual Pigments and Retinal Analogs

PAGE 369

Srinivasan et al. analyze features contributing to optimal receptor-ligand interaction between retinal analogs and two GPCRs that they bind, photoactivated rhodopsin and red cone opsin. The specificity and conformational complementarity between ligand and receptor can have implications for other GPCRs.

Biosynthesis of L-2,3-Diaminopropionic Acid

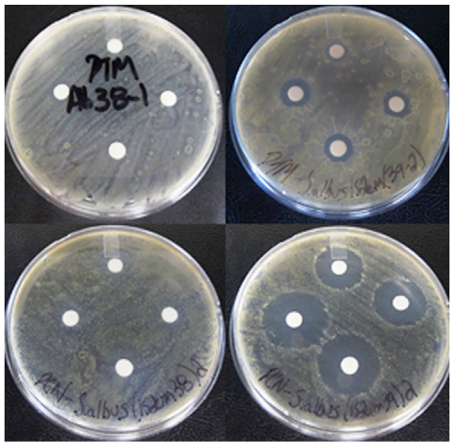
PAGE 379

L-2,3-diaminopropionic acid (L-Dap) is a biosynthetic precursor incorporated into both antibiotics and siderophores. Kobylarz et al. decipher the L-Dap biosynthetic pathway in *Staphylococcus aureus* that is essential for assembly of the siderophore staphyloferrin B and contributes to the iron sparing response.

Two Ways To Become Self-Resistant

PAGE 389

Platensimycin (PTM) and platencin (PTN) are potent inhibitors of bacterial fatty acid synthases. Peterson et al. discover two mechanisms for PTM and PTN resistance in the *Streptomyces platensis* producers. PtmP3/PtnP3 confer resistance by target replacement, while FabF confers resistance by target modification.



A Spironolactone Lends a Helping Hand to Pt Drugs

PAGE 398

Nucleotide excision repair (NER) removes DNA lesions resulting from exposure to platinum-based drugs used in anticancer therapy. Alekseev et al. describe a spironolactone that acts as a potent NER inhibitor and potentiates the cytotoxicity of platinum derivatives towards tumor cells.

Halogen Bonding Controls Selectivity

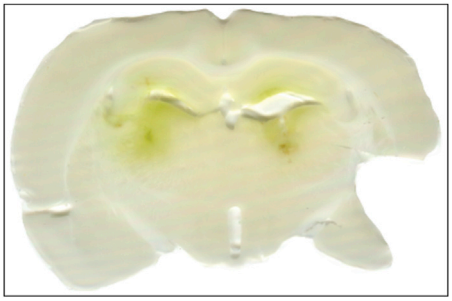
PAGE 408

Due to high similarities between the active sites of the 23 human MMPs, design of selective ligands has been challenging. Tranchant et al. develop a selective FRET substrate of MMP-9, which was obtained by exploiting the ability of halogens to engage in halogen bonding with MMP-9 active site.

Ultra-HTS Way to Evolve Glucose Oxidase

PAGE 414

Ostafe et al. develop an ultra-high-throughput screening system for sorting the glucose oxidase variants using flow cytometry, in vitro compartmentalization, yeast surface display, exogenous delivery of glucose substrate through the oil phase, and covalent labeling of the cells with fluorescein-tyramide.



Resource: A Different Contrast Mechanism

PAGE 422

Westmeyer et al. describe a method for detecting expression of an alkaline phosphatase reporter enzyme using a solubility-switching metalloporphyrin substrate. The contrast mechanism functions in vitro, in brain slices, and in animals and is compatible with optical and magnetic resonance imaging-based readout.

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